

**REMARKS**

Reconsideration of this application is respectfully requested.

**I. Status of the Claims**

Claims 1 and 14 have been amended to specify that proteolytic enzymes in the topical composition are selected from papain, bromelain, pepsin, peptidase, trypsin, enterokinase, alpha-chymotrypsin, and mixtures thereof. Support for these amendments may be found in the specification at, for example, page 8, lines 13-20. Claims 20-23 have been added. Support for these claims may be found in the specification at, for example, page 7, lines 9-10; page 8, lines 18-20; and pages 25-29 (Examples 7-10). No new matter has been added to the application.

Upon entry of this Amendment, claims 1 and 4-23 are pending. Because claims 11-13 have been withdrawn from consideration, only claims 1, 4-10, and 14-23 are currently at issue.

**II. Anticipation Rejection**

Claims 1, 4, 10, and 14-17 have been rejected as anticipated by Elliot et al. (U.S. Patent Application Publication No. 2003/0175232). Elliot relates to stabilized enzyme compositions for topical application. Elliot specifically discloses compositions containing subtilisin BPN', a variant of subtilisin BPN', and subtilisin Carlsberg. *See* paragraph [0163] and Examples I to XI.

In order to advance prosecution and without conceding to the rejection, claims 1 and 14 have been amended to recite that the proteolytic enzymes present in the topical composition are selected from papain, bromelain, pepsin, peptidase, trypsin, enterokinase, alpha-chymotrypsin, and mixtures thereof.

As amended, the pending claims are not anticipated by Elliot because, *inter alia*, Elliot does not disclose topical compositions containing (a) L-carnitine, acyl L-carnitine, or a salt thereof and (b) one or more hydroxy acids, proteolytic enzymes selected from papain, bromelain, pepsin, peptidase, trypsin, enterokinase, alpha-chymotrypsin, and mixtures thereof, skin lightening agents, or

a mixture thereof, wherein the topical composition has a pH of about 6-8. Thus the basis of the rejection is believed to have been obviated. Accordingly, withdrawal of the rejection is respectfully requested.

### **III. Obviousness Rejection**

Claims 1, 4-10, and 14-19 have been rejected as obvious over Paul (U.S. Patent No. 6,149,924) in view of Elliot, Cavazza et al. (EP 0631779 A1), Johnsen et al. (U.S. Patent No. 3,683,939), Vromen (U.S. Patent No. 6,416,769), Yu et al. (U.S. Patent No. 5,589,505), and Deckner et al. (U.S. Patent No. 5,968,528).

The presently claimed topical compositions have been found to exhibit unexpectedly improved exfoliation performance. First, it has been found that L-carnitine compositions with pH values within the range of about 6-8 exfoliate the skin more effectively than compositions at lower pH ranges. *See* page 2, paragraph [6]; page 4, paragraphs [10]-[11]; Example 7, and Fig. 1 of the specification. The exfoliation efficacy of topical compositions containing L-carnitine was tested at pH values ranging from 4.0 to 7.0 over a period of 20 days. In the experiment, dansyl chloride was used as a fluorescent marker for exfoliation efficiency. A control composition was also tested as a comparison. *See* Example 7. Skin was first treated with dansyl chloride, and the presently claimed composition or control composition samples were then applied twice daily to the skin. UV light was used to observe the disappearance of fluorescence intensity over the 20-day period. The elimination of fluorescence was associated with fully exfoliated skin. *See* Figure 1.

As shown in Figure 1, compositions prepared at pH values of 4.0 and 5.0 did not induce significant exfoliation until days 16 and 17, respectively, and further showed minimal improvement over the control composition (33% for both compositions at day 17 compared to 11% for the control). In both samples, exfoliation was not complete until day 19 (compared to day 20 for the control).

On the other hand, significant exfoliation was observed in compositions prepared at pH values of 6.0 and 7.0 at days 13 and 14, respectively. By day 17, exfoliation induced by these samples was complete, whereas exfoliation was only initiated at day 17 in compositions prepared at pH 4.0 and

5.0. Thus, the compositions prepared at pH 6.0 and 7.0 demonstrate superior exfoliating performance over the more acidic compositions.

Second, it was found that L-carnitine exfoliates skin more effectively and faster than racemic (DL) carnitine. *See* page 3, lines 1-2 and paragraph [8]; Example 9, and Fig. 3 of the specification. Using the dansyl chloride assay as described above, the exfoliation performance of compositions containing 2.8% and 5.6% L-carnitine and DL-carnitine was tested. L-carnitine achieved complete exfoliation more rapidly than racemic carnitine at the same concentration.

Additionally, claims 18, 19, 22, and 23 specify that the compositions include the proteolytic enzyme papain. L-carnitine compositions containing papain have been found to exfoliate skin more effectively than compositions containing L-carnitine or papain alone. *See* page 2, paragraph [6]; Example 10; and Fig. 4 of the specification. However, as discussed above, unexpectedly improved exfoliation is not limited to compositions containing both L-carnitine and papain.

Paul, Elliot, Cavazza, Johnsen, Vromen, Yu, and Deckner fail to teach or suggest that a correlation exists between pH and exfoliation performance. Specifically, the references collectively do not disclose or suggest that compositions containing (a) L-carnitine, acyl L-carnitine, or a salt thereof and (b) a hydroxy acid, one of the recited proteolytic enzymes, skin lightening agent, or a mixture thereof at a pH of 6-8 yields improved exfoliating properties. Thus, the skilled artisan would not have expected that adjusting the pH as claimed would produce significantly improved exfoliation.

For at least the above reasons, claims 1, 4-10, and 14-19 are not obvious over the cited references. Applicants respectfully request that the rejection be withdrawn.

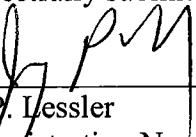
The applicants further respectfully submit that new claims 20-23 are allowable over the cited references for at least the above reasons.

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance. If there are any remaining issues that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment,

the Examiner is kindly requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

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